CANCER THERAPY

BACKGROUND

[0001] Cancer is a leading cause of death worldwide, accounting for 7.6 billion deaths (around 13% of all deaths) in 2008. Lung, stomach, liver, colon, and breast cancer cause the most cancer deaths each year, according to the World Health Organization. Cancer is the second leading cause of death in the United States, exceeded only by heart disease. In 2008, more than 565,000 people died of cancer, and more than 1.48 million people had a diagnosis of cancer, according to the United States Cancer Statistics: 1999-2008 Incidence and Mortality Web-based Report. The cost of cancer extends beyond the number of lives lost and new diagnoses each year. The financial costs of cancer also are overwhelming. According to the National Institutes of Health, cancer cost the United States an estimated $263.8 billion in medical costs and lost productivity in 2010. (See, www.cdc.gov/chronicdisease/resources/publications/AAG/dcpc.htm.)

SUMMARY

[0002] The present invention relates in general to methods and compositions for the treatment of cancer, in some embodiments for the treatment of cancers of epithelial cell origin. Improved treatment methods and regimens described herein are the product of a novel and comprehensive approach to the development of individualized treatments for cancer. The approach to treatment recognizes that cancer growth and metastasis depends on unchecked cellular processes, in particular angiogenesis, and simultaneously the activation of multiple metabolic and signaling pathways in the patient. Pathways that in a normal individual would suppress, or at least not support, cancer growth are inactive, blocked or attenuated in a cancer patient; likewise, pathways that are cancer-supportive, which are held in check or counterbalanced in a normal individual, are amplified in a cancer patient. In some embodiments, an object of the therapeutic approach of the present invention is to inhibit or attenuate angiogenesis as well as to rebalance as many of the metabolic, intercellular signaling, and intracellular signaling pathways that are detected or suspected to be contributing to the survival or growth of the cancer.

[0003] In some particular embodiments, objects of provided treatment protocols described herein are to achieve one or more of the following:

[0004] blocking, interrupting, or attenuating tumor angiogenesis (i.e., the formation and development of the vasculature that tumors need in order to thrive and progress) or pathways that support angiogenesis, including disruption of signaling inducing vasculogenic mimicry (e.g. tumor stem cell activity);

[0005] reducing, blocking, or reversing the mechanisms of chemo-resistance to chemotherapeutic drugs, in order to enhance effectiveness of chemotherapy, preferably while increasing anti-tumor, pro-apoptotic activity;

[0006] supporting a metabolic shift from aerobic glycolysis (the "Warburg Effect") to glucose oxidation, which promotes or renews a capacity for undergoing apoptosis;

[0007] blocking, interrupting, or attenuating intracellular tumor cell signal transduction pathways that promote tumor cell growth;

[0008] inhibiting intercellular signaling pathways that facilitate tumor invasion into local tissues and tumor metastasis (i.e., the spread of tumor cells to other tissues or organs);

[0009] Inducing opioid immune modulation that has an inhibitory effect on cell proliferation. (Donahue R N et al., Low-dose naltrexone targets opioid growth factor receptor pathway to inhibit cell proliferation: mechanistic evidence from tissue culture model, Exp. Biol. Med. (Maywood), 2011 Sep. 1; 236(9); 1036-50)

[0010] reducing or avoiding toxic side effects of chemotherapy and any other active ingredients added to a treatment regimen; and

[0011] augmenting or enhancing the patient's host defenses (particularly the host immune system), their general health and well-being.

[0012] In some embodiments, the present invention provides a unique approach for the treatment of cancer, combining use of one or more agents conventionally included in cancer treatments with administration of one or more naturally-occurring compounds and/or nutrients, e.g., "nutraceuticals".

[0013] In some embodiments, treatment protocols described herein are designed to inhibit, arrest, and/or otherwise disrupt, or, where appropriate, enhance endogenous signaling pathways and/or upregulate anti-angiogenic regulators (such as angiostatin, endostatin, or thrombospodin-1) that, when dysregulated, lead to the formation or support the development of cancerous growth or tumors.

[0014] In a preferred embodiment, the present invention is directed to compositions and methods for the treatment of cancers or tumors that are epithelial cell related.

[0015] In another embodiment, the present invention is designed to prevent the recurrence of cancer, by continuing the disclosed treatment regimen once it has been determined that the cancer or tumor is in remission or, in other words, there is no evidence of disease.

[0016] One unique feature of the method and compositions described herein is that the combination of compounds and dosages of each can be tailored for each individual or patient in order to maximize the benefit realized for that particular patient. In this respect, the treatment regimen will be based on a pretreatment analysis of specific parameters, for example, on an analysis of blood or biopsied tissue obtained from the patient to be treated, prior to initiating the regimen.

[0017] The present invention provides a unique integrative approach to cancer therapy, in which conventional oncology can be merged with complementary modalities. The complementary aspect emphasizes the use of natural compounds and non-chemotherapeutic drugs to facilitate a synergistic approach in which each element of treatment, both conventional and non-conventional, is designed to inhibit angiogenesis and the oncogenic signaling transduction pathways within cancer cells and the intercellular signaling between tumor cells and their local cellular and biochemical microenvironment, with a strong emphasis on disruption of the intercellular signaling that fuels the ongoing processes of tumor angiogenesis.

[0018] The present invention encompasses a variety of novel insights, including defining the sources of various problems associated with certain conventional chemotherapeutic regimens, as described herein.